(m) *Bacterin.* An inactivated bacterial product consisting of an antigenic suspension of organisms or particulate parts of organisms, representing a whole culture or a concentrate thereof, with or without the unevaluated growth products, which has been inactivated as demonstrated by acceptable tests written into the filed Outline of Production for the product.

(n) *Toxoid.* An inactivated bacterial product which consists of a sterile, antigenic toxin or toxic growth product, which has resulted from the growth of bacterial organisms in a culture medium from which the bacterial cells have been removed, which has been inactivated without appreciable loss of antigenicity as measured by suitable tests, and which is nontoxic as demonstrated by acceptable tests written into the filed Outline of Production.

(o) *Bacterin-toxoid.* An inactivated bacterial product which is either:

(1) A suspension of organisms, representing a whole culture or a concentrate thereof, with the toxic growth products from the culture which has been inactivated without appreciable loss of antigenicity as measured by suitable tests, the inactivation of organisms and toxins being demonstrated by acceptable tests written into the filed Outline of Production: *Provided*, That it shall contain cellular antigens and shall stimulate the development of antitoxin; or

(2) A combination product in which one or more toxoids or bacterin-toxoids is combined with one or more bacterins or one or more bacterin-toxoids.

(p) *Bacterial extract.* An inactivated bacterial product which consists of the sterile, nontoxic, antigenic derivatives extracted from bacterial organisms or from culture medium in which bacterial organisms have grown.

[38 FR 8426, Apr. 2, 1973, as amended at 42 FR 63770, Dec. 20, 1977; 50 FR 24903, June 14, 1985; 56 FR 66782, Dec. 26, 1991; 60 FR 14354, Mar. 17, 1995]

§ 101.4 Labeling terminology.

Terms pertaining to identification and packaging of biological products shall mean:

(a) *Label.* All written, graphic, or printed matter:

(1) Upon or attached to a final container of a biological product;

(2) Appearing upon any immediate carton or box used to package such final container; and

(3) Appearing on any accompanying enclosures (leaflets, inserts, or circulars) on which required information or directions as to the use of the biological product shall be found.

(b) *Labeling.* All labels and other written, printed, or graphic matter accompanying the final container.

(c) *Final container.* The unit, bottle, vial, ampule, tube, or other receptacle into which any biological product is filled for distribution and sale.

(d) *True name.* The name entered on the product license or permit at the time of issuance to differentiate the biological product from others: *Provided*, That, the principal part of such name shall be emphasized on such license or permit by being more prominently lettered than descriptive terms which may be necessary to complete the differentiation.

(e) *Serial number.* Numbers or numbers and letters used to identify and distinguish one serial from others.

(f) *Expiration date.* A date designating the end of the period during which a biological product, when properly stored and handled, can be expected with reasonable certainty, to be efficacious.

(g) *Label number.* A number assigned by Animal and Plant Health Inspection Service to each label or sketch submitted for review.

(h) *Master label.* The finished carton, container, or enclosure label for the smallest size final container that is authorized for a biological product, that serves as the Master template label applicable to all other size containers or cartons of the same product that is marketed by a licensee, subsidiary, division, or distributor.

[38 FR 8426, Apr. 2, 1973, as amended at 42 FR 63770, Dec. 20, 1977; 56 FR 66782, Dec. 26, 1991; 61 FR 29464, June 11, 1996]

§ 101.5 Testing terminology.

Terms used when evaluating biological products shall mean:

(a) *Standard Requirement.* Test methods, procedures, and criteria established by Animal and Plant Health Inspection Service for evaluating biological products to be pure, safe, potent, and efficacious, and not to be worthless, contaminated, dangerous, or harmful under the Act.

(b) *Log.* Logarithm computed to the base 10.

(c) *Pure or purity.* Quality of a biological product prepared to a final form relatively free of extraneous micro-organisms and extraneous material (organic or inorganic) as determined by test methods or procedures established by Animal and Plant Health Inspection Service in Standard Requirements or in the approved Outline of Production for such product, but free of extraneous microorganisms or material which in the opinion of the Administrator adversely affects the safety, potency, or efficacy of such product.

(d) *Safe or safety.* Freedom from properties causing undue local or systemic reactions when used as recommended or suggested by the manufacturer.

(e) *Sterile or sterility.* Freedom from viable contaminating microorganisms as demonstrated by procedures prescribed in part 113 of this subchapter, Standard Requirements, and approved Outlines of Production.

(f) *Potent or potency.* Relative strength of a biological product as determined by test methods or procedures as established by Animal and Plant Health Inspection Service in Standard Requirements or in the approved Outline of Production for such product.

(g) *Efficacious or efficacy.* Specific ability or capacity of the biological product to effect the result for which it is offered when used under the conditions recommended by the manufacturer.

(h) *Dose.* The amount of a biological product recommended on the label to be given to one animal at one time.

(i) *Vaccinate.* An animal which has been inoculated, injected, or otherwise administered a biological product being evaluated.

(j) *Control animal.* An animal, which may be referred to as a control, used in a test procedure for purposes of comparison or to add validity to the results.

(k) *Day.* Time elapsing between any regular working hour of one day and any regular working hour of the following day.

(l) *No test.* A test which produces inconclusive or invalid results and therefore, cannot be used to evaluate a biological product.

(m) *Healthy.* Apparently normal in all vital functions and free of signs of disease.

(n) *Unfavorable reactions.* Overt adverse changes which occur in healthy test animals subsequent to initiation of a test and manifested during the observation period prescribed in the test protocol which are attributable either to the biological product being tested or to factors unrelated to such product as determined by the responsible individual conducting the test.

(o) *Master reference.* A Master Reference is a reference whose potency is correlated, directly or indirectly, to host animal immunogenicity. The Master Reference may be used as the working reference in in vitro tests for relative potency. The Master Reference may also be used to establish the relative potency of a serial of product used in requalification studies and to establish the relative potency of working references. The preparation of a Master Reference as described in a filed Outline of Production may be:

(1) A completed serial of vaccine or bacterin prepared in accordance with a filed Outline of Production;

(2) A purified preparation of a protective immunogen or antigen; or

(3) A nonadjuvanted harvested culture of microorganisms.

(p) *Working reference.* A Working Reference is the reference preparation that is used in the in vitro test for the release of serials of product. Working References may be:

(1) Master References; or

(2) Serials of product that have been prepared and qualified, in a manner acceptable to Animal and Plant Health Inspection Service for use as reference preparations.

(q) *Qualifying serial.* (1) A serial of biological product used to test for immunogenicity when the Master or

Working Reference is a purified antigen or nonadjuvanted harvest material. Qualifying serials shall be produced in accordance with the filed Outline of Production, tested for immunogenicity in accordance with methods deemed appropriate by the Animal and Plant Health Inspection Service, and have a geometric mean relative potency, when compared to the Master Reference, of not greater than 1.0 as established by: independent parallel line assays with five or more replicates; or other valid assay methods for determining relative antigen content which demonstrate linearity, specificity, and reproducibility at least equivalent to the parallel line assay and are acceptable to the Animal and Plant Health Inspection Service.

(2) Qualifying serials used to requalify or extend the dating period of a Master Reference shall be determined to be immunogenic in accordance with methods deemed appropriate by the Animal and Plant Health Inspection Service as provided in paragraph (a)(1) of this section, and, in addition, shall be within their permitted dating period and have been prepared in accordance with the production method described in the currently filed Outline of Production.

(r) *Immunogenicity*. The ability of a biological product to elicit an immune response in animals as determined by test methods or procedures acceptable to the Animal and Plant Health Inspection Service.

[38 FR 8426, Apr. 2, 1973, as amended at 40 FR 45419, Oct. 2, 1975; 41 FR 6751, Feb. 13, 1976; 43 FR 3701, Jan. 27, 1978; 56 FR 66782, 66783 Dec. 26, 1991; 62 FR 19037, Apr. 18, 1997]

§ 101.6 Cell cultures.

When used in conjunction with or in reference to cell cultures, which may be referred to as tissue cultures, the following terms shall mean:

(a) *Batches of primary cells*. A pool of original cells derived from normal tissue up to and including the 10th subculture.

(b) *Cell line*. A pool of cells which are 11 or more subcultures from the tissue of origin.

(c) *Subculture*. Each flask to flask transfer or passage regardless of the number of cell replications.

(d) *Master Cell Stock (MCS)*. The supply of cells of a specific passage level from which cells for production of biologics originate.

[38 FR 8426, Apr. 2, 1973, as amended at 40 FR 45419, Oct. 2, 1975; 49 FR 22624, May 31, 1984]

§ 101.7 Seed organisms.

When used in conjunction with or in reference to seed organisms, the following shall mean:

(a) *Master Seed*. An organism at a specific passage level which has been selected and permanently stored by the producer from which all other seed passages are derived within permitted levels.

(b) *Working Seed*. An organism at a passage level between Master Seed and Production Seed.

(c) *Production Seed*. An organism at a specified passage level which is used without further propagation for initiating preparation of a fraction.

[49 FR 22625, May 31, 1984]

PART 102—LICENSES FOR BIOLOGICAL PRODUCTS

Sec.

AUTHORITY: 21 U.S.C. 151–159; 7 CFR 2.22, 2.80, and 371.4.

§ 102.1 Licenses issued by the Administrator.

Each establishment qualified to prepare biological products under the Virus-Serum-Toxin Act shall hold an unexpired and unrevoked U.S. Veterinary Biologics Establishment License issued by the Administrator and a U.S. Veterinary Biological Product License for each product prepared in such establishment unless the product is subject to the provisions of 9 CFR parts 103 or 106 of this subchapter.

[60 FR 48021, Sept. 18, 1995]